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Preoperative inspiratory muscle training prevents pulmonary complications after cardiac surgery – a systematic review

Emil Osman Thybo Karanfil & Ann Merete Møller

ABSTRACT

INTRODUCTION: Post-operative pulmonary complications are a common cause of morbidity and mortality in patients undergoing heart surgery. The aim of this systematic review was to determine if preoperative inspiratory muscle training could prevent the development of pneumonia and atelectasis in patients undergoing coronary artery bypass grafting (CABG) or heart valve surgery.

METHODS: Systematic searches were performed in MEDLINE, Embase and the Cochrane Library. The included studies compared the development of pneumonia and atelectasis in CABG patients or heart valve surgery patients who were prescribed either preoperative inspiratory muscle training or usual care. The quality of the studies was assessed using the Cochrane Risk of Bias Tool.

RESULTS: The search yielded 2,479 records. The inclusion criteria were fulfilled by five studies. All the studies were randomised controlled trials. We found that the development of both pneumonia and atelectasis was significantly reduced among patients who received inspiratory muscle training preoperatively compared with patients treated with usual care.

CONCLUSIONS: Preoperative inspiratory muscle training may reduce the risk of developing pneumonia and atelectasis. However, more trials are needed to support and strengthen the evidence found in this systematic review before routine implementation of this kind of training preoperatively.

Post-operative pulmonary complications are among the most common causes of morbidity and mortality in patients undergoing open heart surgery and cardiopulmonary bypass [1, 2]. The complications include atelectasis, pulmonary infections such as pneumonia and bronchitis, pleural effusion, pulmonary oedema, respiratory insufficiency, exacerbation of chronic lung disease, bronchospasm and other types of respiratory insufficiency [2, 3]. These conditions may contribute to inhibited gas exchange due to decreased ventilation efficiency. Several factors have been suggested to influence the development of such complications including the type and duration of surgery, with cardiopulmonary bypass as an important contributor to post-operative pulmonary dysfunction. Among other factors are sternotomy,

wound pain and drain discomfort as well as the residual anaesthetic effect and the patient's pre-operative condition [3, 2]. Thus patients with inhibited preoperative respiration could be at an increased risk of developing post-operative pulmonary complications [4]. This may be explained by insufficient diaphragmatic breathing or by the respiratory fatigue that some patients experience during the post-operative period which could cause alveoli to collapse or sputum clearance to deteriorate [4, 5]. Preoperative training of the respiratory muscles could potentially limit the decrease in respiratory power and endurance seen after cardiac surgery and therefore prevent the development of post-operative pulmonary complications [6].

Previous studies have focused primarily on rehabilitation of the respiratory musculature after heart surgery. Inspiratory muscle training as a form of preoperative conditioning may be another approach to limiting the incidence of post-operative pulmonary complications. With this approach, the patient receives preoperative training of the inspiratory muscles in order to improve muscle strength and endurance. In theory, this would increase the baseline of strength and endurance to a higher level prior to surgery, leading to less decrease in respiratory efficiency and hence a lower risk of developing post-operative pulmonary complications.

Inspiratory muscle training consists in applying resistance during the inspiratory phase of the breathing cycle [7]. A training effect is achieved by gradually increasing the resistance. Several methods have been used to perform inspiratory muscle training, including inspiratory threshold pressure loading, isocapnic/nor-

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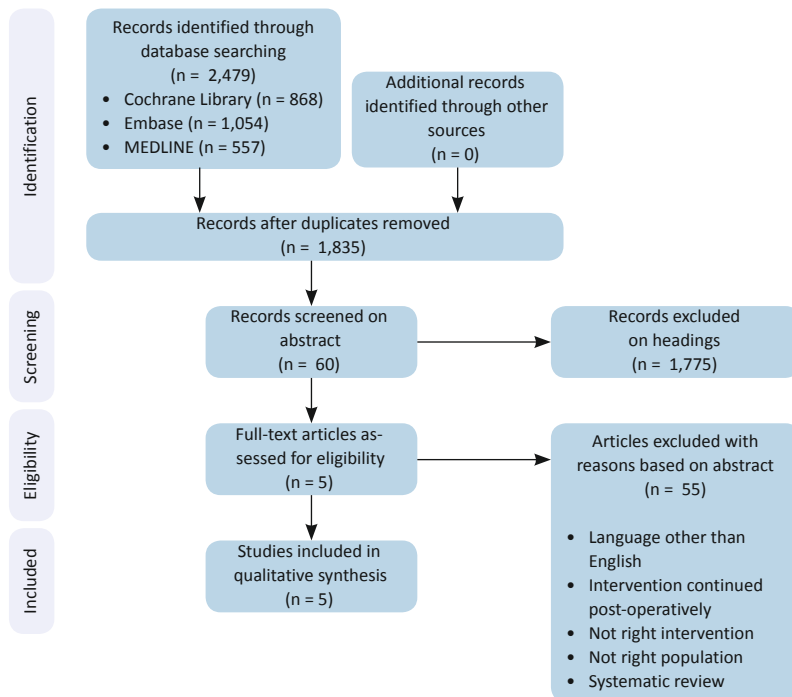


KEY POINTS

- Development of pulmonary complications after coronary artery bypass grafting and heart valve surgery is an important problem that needs attention.
- Preoperative inspiratory muscle training may prevent development of pneumonia and atelectasis after coronary artery bypass grafting and heart valve surgery.
- More studies are needed to firmly establish the current indication that preoperative inspiratory muscle training is safe and effective in reducing the incidence of postoperative pulmonary complications.

 **FIGURE 1**

Study flow diagram (PRISMA).



nocapnic hyperpnoea and inspiratory resistive flow loading [8]. Studies have shown that inspiratory muscle training is simple and that it can be performed at home after instruction during the preoperative period [6, 9]. Thus, inspiratory muscle training may contribute to a better perioperative treatment of the cardiac patient and better resource utilisation.

The aim of the present study was to systematically review if inspiratory muscle training prior to cardiac surgery compared with usual care (sham training, no inspiratory muscle training) can diminish the incidence of post-operative pulmonary complications such as pneumonia and atelectasis.

METHODS

We submitted the protocol for this systematic review to the International Prospective Register of Systematic Reviews (PROSPERO – registration number: CRD42016048964) prior to its submission for publication. This systematic review was prepared in accordance with the PRISMA guidelines [10].

The inclusion criteria were randomised controlled trials that contained any kind of preoperative inspiratory muscle training compared with usual care, a placebo intervention or no inspiratory muscle training. Only studies published in English were included. The population was adults (> 50 years) of both genders awaiting

elective cardiac surgery (CABG or heart valve replacement). Inspiratory muscle training could be achieved through inspiratory threshold pressure loading, isocapnic/normocapnic hyperpnoea or inspiratory resistive flow loading [8]. We explored the following outcomes:

- Post-operative development of pneumonia
- Post-operative development of atelectasis.

Studies were excluded if preoperative inspiratory muscle training was combined with any other kind of training other than usual care, or if the intervention continued post-operatively. Studies that focused on non-cardiac patients were also excluded.

The databases MEDLINE, Embase and Cochrane Library were scrutinised for relevant studies. Searches were run from the year and month that each database became operational until September 2017. When necessary, we contacted trial authors for additional information. Furthermore, reference lists and citations of included articles were reviewed to identify publications not retrieved by the electronic search.

We developed a subject-specific search strategy in MEDLINE (see the text box) and used that as the basis for the search strategies in the other databases listed. Where appropriate, the search strategy was expanded with search terms identifying, randomised controlled trials, (RCTS). All search strategies can be found in Appendix A [11].

We scanned <https://clinicaltrials.gov> for ongoing and unpublished trials (30 September 2017):

1. exp exercise/ or exp Physical Therapy Modalities/ or exp Motor Activity/ or Physical Fitness/ or exp Exercise Therapy/ or exercise*.mp. or (physical adj3 (activit* or therap*)).mp. or fitness.mp. or training.mp. or walk*.mp. or prehab*.mp. or sport*.mp. or physio*.mp. or cycl*.mp. or aerobic*.mp. or swim*.mp. or motion.mp. or movement.mp. or flexibility.mp. or stretch*.mp.
2. exp preoperative care/ or exp preoperative period/ or preoperati*.mp. or prehabilita*.mp. or pre-habilita*.mp. or preoperat*.mp. or pre-operat*.mp. or presurg*.mp. or pre-surg*.mp. or before surg*.mp. or prior to surg*.mp.
3. exp Cardiovascular Surgical Procedures/ or exp Thoracic Surgery/ or ((Vascular or cardiac or cardio or Cardiovascular or Coronary or aort* or thora* or heart*) adj5 Surg*).mp.
4. ((randomized controlled trial or controlled clinical trial).pt. or randomi?ed.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.) not (exp animals/ not humans.sh.)
5. 1 and 2 and 3 and 4.

We scanned the reference lists and the citations of the included trials and any relevant systematic reviews identified for further references to additional trials.

Two researchers screened all articles that were found using the aforementioned search strategy. Studies were screened by headings, and their abstracts were read provided they described the intervention or population used in this review. The two researchers independently reviewed the full text of all the eligible studies and extracted data onto a data extraction sheet to assess for risk of bias using The Cochrane Risk of Bias Tool [12]. Discrepancy between the two reviewers was resolved through discussion until a consensus was reached.

Data from the eligible studies were extracted onto a preformatted sheet consisting of divisions for name of study and first author, publication year, characteristics and number of contenders, design of intervention, comparison and outcome. If data were incomplete or some data were missing, the authors of the studies were contacted. Finally, the data were examined in Review Manager 5.3 [13] and used to produce forest plots for the two outcome measures.

Measures of treatment effects

We performed all comparisons between the preoperative inspiratory muscle training (IMT) and usual care. As measure of the effect of intervention, we calculated the risk ratio for dichotomous outcomes.

Assessment of heterogeneity

We initially assessed for heterogeneity by visual inspection of the results of the two forest plots. We measured statistical heterogeneity using the I^2 in Review Manager 5.3 [13]. Both forest plots showed $I^2 = 0\%$ (no statistical heterogeneity).

Assessment of reporting bias

We planned to do a funnel plot to assess for reporting bias if more than ten studies were found. However, we did not reach this number of studies, and therefore we decided not to prepare the funnel plot.

Data synthesis

As the included studies were sufficiently homogeneous, we were able to make forest plots for both pneumonia and atelectasis. We calculated risk ratio as an effect measure and its associated 95% confidence interval (CI) because it was interpretable and generalisable.

RESULTS

Study selection

The database search yielded 2,479 articles. We found no articles through other sources. Of these, 644 were identified as duplicates. Thus 1,835 articles were screened, from which 1,775 were excluded entirely based on their headings. The abstracts of the remaining 60 articles were scrutinised. Those that were published in a language other than English or had the intervention running post-operatively were excluded. Systematic reviews and studies with a population other than cardiac patients or who used another intervention than inspiratory muscle training were also excluded. The remaining five studies were retrieved in full text and assessed for potential eligibility. All five studies were included in the final qualitative analysis. All five studies were randomised controlled trials. Thus, the total number of patients included in the analysis was 451, see **Figure 1**.

Risk of bias in included studies

The included studies were assessed for bias using The Cochrane Risk of Bias Tool [14], see **Table 1**.

Two trials used adequate methods for random sequence generation [9, 15] and two studies stated that random sequence generation was applied, but failed to describe this sufficiently well [16, 17], and it was unknown whether random sequence generation had been used in the final study [18]. Two trials used allocation concealment [9, 15], whereas three studies did not report on this [16-18].

Due to the nature of the intervention, it was difficult to blind the participants and personnel in all trials. However, one study reported using a sham intervention where the control group used the same training device



TABLE 1

Risk of bias: the criteria were satisfied, yes, no or unknown.

Reference	Selection bias		Performance bias: blinding of participants and personnel	Detection bias: blinding of outcome assessment	Attrition bias: incomplete outcome data	Reporting bias: selective reporting	Other bias: anything else
	random sequence generation	allocation concealment					
Hulzebos et al, 2006 [9]	Yes	Yes	No	Yes	Yes	Unknown	Yes
Hulzebos et al, 2006 [15]	Yes	Yes	No	Yes	Yes	Yes	Yes
Carvalho et al, 2011 [18]	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Weiner et al, 1998 [16]	No	Unknown	Yes	Unknown	Unknown	Unknown	Yes
Ferreira et al, 2009 [17]	No	Unknown	No	Unknown	Yes	Unknown	Yes

TABLE 2

Study characteristics.

Reference	Study type	Characteristics	Subjects, N (men/women) n (mean age \pm SD)	Intervention	Comparison	Results
Hulzebos et al, 2006 [15]	RCT	Candidates for CABG surgery at high risk of PPCs	276 (215/61) I: 139 (67 \pm 9.0) C: 137 (67 \pm 9.2)	IMT starting at 30% of the patient's Pi-max IMT 20 min. a day, 7 days a week for \geq 2 wks 6 days a wk without supervision and 1 day with supervision If RPE was < 5 resistance was increased incrementally by 5% Education on incentive spirometry, active cycle of breathing techniques, forced expiration techniques	Instruction in deep breathing manoeuvres, coughing and early mobilisation defined as usual care Only C group received this and only 1 day prior to surgery	PPC grade \geq 2: I: 25 (18%) vs. C: 48 (35%), $p = 0.02$ Pneumonia: I: 9 (6.5%) vs. C: 22 (16.1%), $p = 0.01$ Atelectasis: I: 14 vs. C: 18 Median LOS: I: 7 (range: 5-41) vs. C: 8 (range: 6-70), $p = 0.02$
Hulzebos et al, 2006 [9]	RCT	Candidates for elective CABG surgery	26 (13/13) I: 14 (70.14 \pm 9.9) C: 12 (70.5 \pm 10.1)	IMT starting at 30% of the patient's Pi-max, each day, 20 min a day for \geq 2 wks 1 session/wk was supervised The other 6 sessions/wk were unsupervised If RPE was < 5 resistance was increased incrementally by 2 cm H ₂ O	Education about early mobilisation and coughing with wound support 1 day before surgery defined as usual care	Pneumonia: I: 1 vs. C: 1, NS Atelectasis: I: 2 (14.2%) vs. C: 6 (50%), $p = 0.05$ Median LOS: I: 7.93 (SD \pm 1.94) vs. C: 9.92 (SD \pm 5.78), $p = 0.24$
Weiner et al, 1998 [16]	RCT	Candidates for elective CABG surgery	84 (58/26) I: 42 (59 \pm 3.8) C: 42 (6 \pm 3.1)	IMT, resistance starting at 15% of the patient's Pi-max progressing up to 60% of Pi-max, 6 days/wk, 2-4 wks Each session consisted of 0.5 h under supervision of a physician	Sham training, IMT with no resistance, 6 days/wk, 2-4 wks	Pneumonia: I: 1 (3.4%) vs. C: 3 (7.14%), NS Pleural effusion: I: 5 (11.9%) vs. C: 3 (7.1%) Hemidiaphragmatic paralysis: I: 2 (4.8%) vs. C: 3 (7.1%)
Ferreira et al, 2009 [17]	RCT	Candidates for elective CABG or cardiac valve surgery	30 (22/8) I: 15 (62.47 \pm 8.06) C: 15 (63.07 \pm 7.93)	Patients were instructed to perform 5 series of 10 calm and deep inspirations with at least 1-min. intervals between the series, without feeling tired or sick, with the incentive of a respiratory instrument Threshold IMT, with a load of 40% of MaxIP (D0)15 The series were to be repeated 3 \times daily while waiting for the surgery Waiting time for surgery were \geq 2 wks The average time available for respiratory training was 154.0 \pm 87.4 days	The other 15 patients received general advice and did not train the inspiratory muscle	Pneumonia: I: 1 (6.7%) vs. C: 0 (0%), NS
Carvalho et al, 2011 [18]	RCT	Candidates for elective CABG surgery	n = 32 (21/11) I: 16 (62 \pm 9.9) C: 16 (62 \pm 10.9)	The IMT in I group was performed with the set Threshold IMT with workload set to 30% of the MIP, during the 2 wks prior to surgery Training was performed 7 days/wk, 2 \times a day, 3 sets of 10 repetitions	Unknown	Pneumonia: I: 5.3% vs. C: 12.3%, $p = 0.04$ Atelectasis: I: 18.7% vs. C: 43.2%, $p = 0.02$

C = control; CABG = coronary artery bypass grafting; I = intervention; IMT = inspiratory muscle training; LOS = length of stay; MIP = maximum inspiratory pressure; NS = non-significant; Pi-max = maximum inspiratory pressure; PPC = post-operative pulmonary complication; RCT = randomised controlled trial; RPE = rating of perceived exertion; SD = standard deviation.

as the intervention group, but without applying any resistance [16]. The rest had no blinding of participants or personnel.

Two studies blinded the assessment of the outcome [9, 15]. This was achieved by blinding the physiotherapist with respect to group allocation before the therapist collected the medical records or scored the degree of lung complications. The rest reported either no blinding of the outcome assessment, or it was unknown to which degree this had been taken into account.

Three trials adequately reported information regarding loss to follow-up [9, 15, 17]. In one trial, the proportion of loss to follow-up was limited and similar in both groups [15]. The remaining two studies provided

no description of this [16, 18].

Furthermore, the quality of the included studies was graded using the scoring system by Grading of Recommendations, Assessment, Development and Evaluations [19]. Only one study was graded as "moderate" [15], another study was graded as "low" [9] and the remaining three studies were graded as "very low" [16-18].

Study characteristics

Table 2 presents highlighted study features. All five studies were randomised controlled trials [9, 15-18]. Median study size was 32 (range: 26-276), which could be divided into intervention group 16 (range: 14-139)

and control group 16 (range: 12-137). Thus, one study [15] contained more than 200 participants, and four studies [15-18] included less than 100 participants. Male gender accounted for the main part of the subjects of each trial with a median study size of 22 (range: 13-215), whereas female gender presented a median study size and range of 13 (range: 8-61).

Four studies [9, 15, 16, 18] had only CABG patients in their population, and one [17] study investigated a population comprising both CABG patients and patients undergoing heart valve surgery.

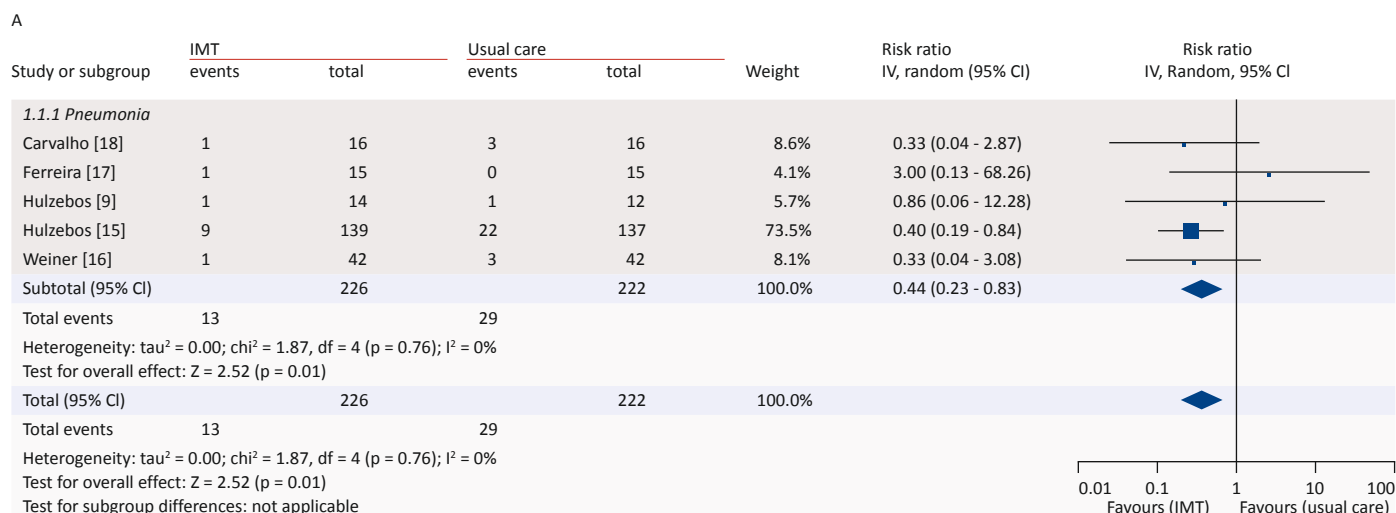
Post-operative pulmonary complications

All studies examined the effect of preoperative inspiratory muscle training on the development of post-operative pneumonia, see **Figure 2A**. Two studies [15, 18] reported a significant reduction ($p \leq 0.05$) in the incidence of pneumonia (the intervention groups: 6.5% and 5.3% versus the control groups: 16.1% and 12.3%, respectively). One study [16] showed a non-significant trend towards less development of pneumonia in the intervention group than in the control group (the intervention groups: 3.4% and 1.1% versus the control groups: 7.1% and 3.2%, respectively). One study [9] had an equal incidence of pneumonia among both its intervention and control group, and one study [17] reported a non-significantly higher incidence of pneumonia in the intervention group (6.7%) than in the control group (0%). Thus, the overall effect of preoperative inspiratory muscle training on development of pneumonia compared with usual

care, see **Figure 2A**. Two studies [15, 18] reported a significant reduction ($p \leq 0.05$) in the incidence of pneumonia (the intervention groups: 6.5% and 5.3% versus the control groups: 16.1% and 12.3%, respectively). One study [16] showed a non-significant trend towards less development of pneumonia in the intervention group than in the control group (the intervention groups: 3.4% and 1.1% versus the control groups: 7.1% and 3.2%, respectively). One study [9] had an equal incidence of pneumonia among both its intervention and control group, and one study [17] reported a non-significantly higher incidence of pneumonia in the intervention group (6.7%) than in the control group (0%). Thus, the overall effect of preoperative inspiratory muscle training on development of pneumonia compared with usual

FIGURE 2

A. Forest plot of comparison: preoperative inspiratory muscle training versus usual care, non-exercise intervention. Outcome: pneumonia. **B.** Forest plot of comparison: preoperative inspiratory muscle training versus usual care, non-exercise intervention. Outcome: atelectasis.



CI = confidence interval; IMT = inspiratory muscle training.



CI = confidence interval; IMT = inspiratory muscle training.

care or no intervention was significant ($p = 0.01$) and showed a risk ratio of 0.44 with a 95% CI of 0.23-0.83.

Three studies [9, 15, 18] reported on the incidence of atelectasis of which two [9, 18] had a significantly higher incidence in the control group than in the intervention group (the intervention groups: 14.2% and 18.7% versus the control groups: 50% and 43.2%), see Figure 2B. Thus, the overall effect of preoperative inspiratory muscle training on development of atelectasis compared with usual care or no intervention was significant ($p = 0.05$) and showed a risk ratio of 0.59 with a 95% CI of 0.35-1.0.

One study [16] reported on pleural effusion (intervention group: 11.9% versus control group: 7.1%) and hemidiaphragmatic paralysis (intervention group: 4.8% versus control group: 7.1%).

The visual inspection of both Figure 2A and B showed little or no heterogeneity. Calculating I^2 showed 0% heterogeneity.

DISCUSSION

This systematic review shows that preoperative inspiratory muscle training results in a significant reduction in both pneumonia and atelectasis in patients undergoing either CABG or cardiac valve surgery. Although we did not include length of stay as an outcome, two studies [9, 15] reported on length of stay after surgery. The effect of preoperative inspiratory muscle training on post-operative length of stay was inconclusive. One study [15] concluded that length of stay was significantly reduced in the intervention group, and the overall effect of the two studies was insignificant ($p = 0.75$). Standard deviation was calculated [20] in one study [15] since length of stay was described as mean (range).

Although the mean estimate of the pooled effect on post-operative pneumonia risk was 56%, the 95% CI does not exclude the possibility that the true effect could be larger or smaller than this (Figure 2A). Even an effect as small as 17% risk reduction in developing post-operative pulmonary complication would still make sense to implement in the clinic considering the simplicity of the intervention. As for the forest plot examining the risk for development of atelectasis, the mean estimate of the pooled effect was 41% (Figure 2B). Although the effect was smaller, it still suggests a positive effect of inspiratory muscle training prior to surgery.

A problem with our interpretation of these results is that the included studies used a variety of different diagnostic tools. Thus, two studies [9, 18] defined pulmonary complications using an operational scale with four classification groups [21] and had a blinded microbiologist assess samples indicative of pneumonia or bronchitis using the criteria of The Centres for Disease Control and Prevention [22]. One study [16] used only X-ray for de-

tection and definition of pulmonary complications, and one study [17] did not state how pulmonary complications were diagnosed. One study [9] diagnosed post-operative pulmonary complications according to clinical symptoms and physical examination and used the radiological criteria for bronchitis, atelectasis and pneumonia defined by Chumillas et al [23]. The lack of diagnostic regimentation across the studies makes it difficult to compare and interpret the results. A review of three different diagnostic tools showed significant variability in the incidence of post-operative pulmonary complications depending upon which tool is used [24]. Thus, drawing conclusion based on present findings should be done with caution.

This review focused on cardiac patients and included studies with elective patients for both CABG and cardiac valve surgery. We chose to include RCTs with any kind of cardiac surgery since the amount of knowledge and material in this field was limited. It is possible that focusing on a specific type of surgery instead of cardiac patients overall would affect the outcome or at least give a more precise picture of how the intervention would work in a given population. However, two other systematic reviews [25, 26], using a more diverse population than ours, but focusing on the same intervention and outcome, reported results pointing the same direction as the ones we have reported in this review. Another problem with our chosen population was that some patients of the included studies [9, 15, 18] were categorised as being at high risk of developing pulmonary complications, whereas others were not [16, 17]. A recent systematic review [26] used a post-hoc meta-analysis and found indication for a stronger effect of training when only trials with patients at a high risk of developing post-operative pulmonary complications were included.

Through our search we also found one large observational study [27] which examined the same population and intervention as the RCTs included in this systematic review. We chose not to include the study in our analysis due to the high risk of bias in an observational study. Although not significant, the study showed the same trend with less development of pneumonia in the intervention group than in the control group.

Although preoperative inspiratory muscle training seems to decrease the risk of developing post-operative pulmonary complications, it remains unknown which training regime is more effective. All studies included in this review had the intervention group performing threshold pressure loading (Table 2). Devices from three different companies were used. The initial training load was between 15% and 40% of the patients' maximal inspiratory load capacity, and progression was achieved through incremental workload increases. We did not fo-

cus on measurements of training effectiveness in this review, but only on clinical outcome. Therefore, we do not know if training effectiveness was associated with clinical outcome. Also, the necessary duration of inspiratory muscle training in order to get a positive training effect and hence a lower incidence of post-operative pulmonary complications is unknown. Training lasted a minimum of two weeks, but most patients were enrolled in a training programme for a longer period than this, making it difficult to settle a lower limit for future training regimes. Two studies [9, 15] reported that training during a week was supervised once, and one study [16] stated that every training session was supervised by a physician. The rest of the included studies [17, 18] had the patients train without weekly supervision. This leaves the possibility that the inspiratory training was performed incorrectly or at least not as efficiently as would be possible with physician supervision. An evaluation of how much supervision this training method would need in order to be performed in the same way and have an effect should also be considered for future studies. Taken together, further research is needed in order to set standards for inspiratory muscle training before its implementation in the clinic.

The search strategy in this systematic review was chosen in order to make the search criteria broad enough to retrieve all articles relevant to the current subject. The search did not include any words directly describing inspiratory muscle training, but rather used words indicative of any training intervention applied pre-operatively for cardiac patients. This yielded a total of 2,479 articles, which we expected to include the relevant literature. We cannot exclude that other relevant articles may exist in other languages or in other databases than the ones used in this review. We choose to do our search in MEDLINE, Embase and Cochrane Library since these databases are widely used in medical research and among medical practitioners, and we therefore consider the search to be fairly thorough. Future research into this subject could consider including other databases as well as studies published in languages other than English, thereby eliminating the risk of language bias.

CONCLUSIONS

Preoperative inspiratory muscle training may reduce the risk of developing post-operative pulmonary complications such as pneumonia and atelectasis following CABG and heart valve surgery. However, more trials are needed to support and strengthen the evidence found in this systematic review before preoperative routine implementation of this kind of training.

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

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